



SEQUENCE LISTING

<110> Serrero, Ginette

<120> 88 KDA TUMORIGENIC GROWTH FACTOR AND ANTAGONISTS

<130> Z9996.488/P001-A

<140> 08/991,862

<141> 1997-12-16

<150> 08/863,862

<151> 1997-05-23

<160> 17

<170> PatentIn Ver. 2.0

<210> 1

<211> 2137

<212> DNA

<213> Mouse epithelin/granulin

<220>

<221> CDS

<222> (23)..(1789)

<223> The sequence is identical to that of the published
mouse granulin except for one nucleotide (T
instead of G) at position 1071 of GP88 cDNA
(position 1056 of mouse granulin).

<400> 1

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gcg	gca	ggg	ctg	gta	gcc	gga	aca	cag	tgt	cca	gat	ggg	cag	ttc	tgc	100
Ala	Ala	Gly	Leu	Val	Ala	Gly	Thr	Gln	Cys	Pro	Asp	Gly	Gln	Phe	Cys	
			15						20					25		
cct	gtt	gcc	tgc	tgc	ctt	gac	cag	gga	gga	gcc	aac	tac	agc	tgc	tgt	148
Pro	Val	Ala	Cys	Cys	Leu	Asp	Gln	Gly	Gly	Ala	Asn	Tyr	Ser	Cys	Cys	
			30						35					40		
aac	cct	ctt	ctg	gac	aca	tgg	cct	aga	ata	acg	agc	cat	cat	cta	gat	196
Asn	Pro	Leu	Leu	Asp	Thr	Trp	Pro	Arg	Ile	Thr	Ser	His	His	Leu	Asp	
			45					50					55			
ggc	tcc	tgc	cag	acc	cat	ggc	cac	tgt	cct	gct	ggc	tat	tct	tgt	ctt	244
Gly	Ser	Cys	Gln	Thr	His	Gly	His	Cys	Pro	Ala	Gly	Tyr	Ser	Cys	Leu	
			60				65					70				
ctc	act	gtg	tct	ggg	act	tcc	agc	tgc	tgc	ccg	ttc	tct	aag	ggt	gtg	292
Leu	Thr	Val	Ser	Gly	Thr	Ser	Ser	Cys	Cys	Pro	Phe	Ser	Lys	Gly	Val	
			75				80				85				90	
tct	tgt	ggt	gat	ggc	tac	cac	tgc	tgc	ccc	cag	ggc	ttc	cac	tgt	agt	340
Ser	Cys	Gly	Asp	Gly	Tyr	His	Cys	Cys	Pro	Gln	Gly	Phe	His	Cys	Ser	
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gca gat ggg aaa tcc tgc ttc cag atg tca gat aac ccc tgc ggt gct 388
Ala Asp Gly Lys Ser Cys Phe Gln Met Ser Asp Asn Pro Leu Gly Ala
110 115 120

gtc cag tgt cct ggg agc cag ttt gaa tgt cct gac tct gcc acc tgc 436
Val Gln Cys Pro Gly Ser Gln Phe Glu Cys Pro Asp Ser Ala Thr Cys
125 130 135

tgc att atg gtt gat ggt tgc tgg gga tgt tgt ccc atg ccc cag gcc 484
Cys Ile Met Val Asp Gly Ser Trp Gly Cys Cys Pro Met Pro Gln Ala
140 145 150

tct tgc tgt gaa gac aga gtg cat tgc tgt ccc cat ggg gcc tcc tgt 532
Ser Cys Cys Glu Asp Arg Val His Cys Cys Pro His Gly Ala Ser Cys
155 160 165 170

gac ctg gtt cac aca cga tgc gtt tca ccc acg ggc acc cac acc cta 580
Asp Leu Val His Thr Arg Cys Val Ser Pro Thr Gly Thr His Thr Leu
175 180 185

cta aag aag ttc cct gca caa aag acc aac agc gca gtg tct ttg cct 628
Leu Lys Lys Phe Pro Ala Gln Lys Thr Asn Ser Ala Val Ser Leu Pro
190 195 200

ttt tct gtc gtg tgc cct gat gct aag acc cag tgt ccc gat gat tct 676
Phe Ser Val Val Cys Pro Asp Ala Lys Thr Gln Cys Pro Asp Asp Ser
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acc tgc tgt gag cta ccc act ggg aag tat ggc tgc tgt cca atg ccc 724
Thr Cys Cys Glu Leu Pro Thr Gly Lys Tyr Gly Cys Cys Pro Met Pro
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Asn Ala Ile Cys Cys Ser Asp His Leu His Cys Cys Pro Gln Asp Thr
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gta tgt gac ctg atc cag agt aag tgc cta tcc aag aac tac acc acg 820
Val Cys Asp Leu Ile Gln Ser Lys Cys Leu Ser Lys Asn Tyr Thr Thr
255 260 265

gat ctc ctg acc aag ctg cct gga tac cca gtg aag gag gtg aag tgc 868
Asp Leu Leu Thr Lys Leu Pro Gly Tyr Pro Val Lys Glu Val Lys Cys
270 275 280

gac atg gag gtg agc tgc cct gaa gga tat acc tgc tgc cgc ctc aac 916
Asp Met Glu Val Ser Cys Pro Glu Gly Tyr Thr Cys Cys Arg Leu Asn
285 290 295

act ggg gcc tgg ggc tgc tgt cca ttt gcc aag gcc gtg tgt tgt gac 964
Thr Gly Ala Trp Gly Cys Cys Pro Phe Ala Lys Ala Val Cys Cys Asp
300 305 310

gat cac att cat tgc tgc ccg gca ggg ttt cag tgt cac aca gag aaa 1012
Asp His Ile His Cys Cys Pro Ala Gly Phe Gln Cys His Thr Glu Lys
315 320 325 330

gga acc tgc gaa atg ggt atc ctc caa gta ggg tgg atg aag aag gtc 1060
Gly Thr Cys Glu Met Gly Ile Leu Gln Val Gly Trp Met Lys Lys Val
335 340 345

ata gcc ccc ctc cgc ctg cca gac cca cag atc ttg aag agt gat aca 1108
 Ile Ala Pro Leu Arg Leu Pro Asp Pro Gln Ile Leu Lys Ser Asp Thr
 350 355 360

cct tgt gat gac ttc act agg tgt cct aca aac aat acc tgc tgc aaa 1156
 Pro Cys Asp Asp Phe Thr Arg Cys Pro Thr Asn Asn Thr Cys Cys Lys
 365 370 375

ctc aat tct ggg gac tgg ggc tgc tgt ccc atc cca gag gct gtc tgc 1204
 Leu Asn Ser Gly Asp Trp Gly Cys Cys Pro Ile Pro Glu Ala Val Cys
 380 385 390

tgc tca gac aac cag cat tgc tgc cct cag ggc ttc aca tgt ctg gct 1252
 Cys Ser Asp Asn Gln His Cys Cys Pro Gln Gly Phe Thr Cys Leu Ala
 395 400 405 410

cag ggg tac tgt cag aag gga gac aca atg gtg gct ggc ctg gag aag 1300
 Gln Gly Tyr Cys Gln Lys Gly Asp Thr Met Val Ala Gly Leu Glu Lys
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 Lys Gly Ser Trp Ala Cys Cys Gln Leu Pro His Ala Val Cys Cys Glu
 460 465 470

gac cgg cag cac tgt tgc ccg gcc ggg tac acc tgc aac gtg aag gcg 1492
 Asp Arg Gln His Cys Cys Pro Ala Gly Tyr Thr Cys Asn Val Lys Ala
 475 480 485 490

agg acc tgt gag aag gat gtc gat ttt atc cag cct ccc gtg ctc ctg 1540
 Arg Thr Cys Glu Lys Asp Val Asp Phe Ile Gln Pro Pro Val Leu Leu
 495 500 505

acc ctc ggc cct aag gtt ggg aat gtg gag tgt gga gaa ggg cat ttc 1588
 Thr Leu Gly Pro Lys Val Gly Asn Val Glu Cys Gly Glu Gly His Phe
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tgc cat gat aac cag acc tgt tgt aaa gac agt gca gga gtc tgg gcc 1636
 Cys His Asp Asn Gln Thr Cys Cys Lys Asp Ser Ala Gly Val Trp Ala
 525 530 535

tgc tgt ccc tac cta aag ggt gtc tgc tgt aga gat gga cgt cac tgt 1684
 Cys Cys Pro Tyr Leu Lys Gly Val Cys Cys Arg Asp Gly Arg His Cys
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 Cys Pro Gly Gly Phe His Cys Ser Ala Arg Gly Thr Lys Cys Leu Arg
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aag aag att cct cgc tgg gac atg ttt ttg agg gat ccg gtc cca aga 1780
 Lys Lys Ile Pro Arg Trp Asp Met Phe Leu Arg Asp Pro Val Pro Arg
 575 580 585

ccg cta ctg taaggaaggg ctacagactt aaggaactcc acagtcctgg 1829
Pro Leu Leu

gaaccctgtt ccgaggggtac ccactactca ggcctcccta gcgcctcttc ccctaacgtc 1889
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accttctttt atggaagaa ggctctggcc aaaagccccg tatcaaactg ccatttcttc 2009
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aaaaaaaa 2137

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<213> Mouse epithelin/granulin

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35 40 45
Trp Pro Arg Ile Thr Ser His His Leu Asp Gly Ser Cys Gln Thr His
50 55 60
Gly His Cys Pro Ala Gly Tyr Ser Cys Leu Leu Thr Val Ser Gly Thr
65 70 75 80
Ser Ser Cys Cys Pro Phe Ser Lys Gly Val Ser Cys Gly Asp Gly Tyr
85 90 95
His Cys Cys Pro Gln Gly Phe His Cys Ser Ala Asp Gly Lys Ser Cys
100 105 110
Phe Gln Met Ser Asp Asn Pro Leu Gly Ala Val Gln Cys Pro Gly Ser
115 120 125
Gln Phe Glu Cys Pro Asp Ser Ala Thr Cys Cys Ile Met Val Asp Gly
130 135 140
Ser Trp Gly Cys Cys Pro Met Pro Gln Ala Ser Cys Cys Glu Asp Arg
145 150 155 160
Val His Cys Cys Pro His Gly Ala Ser Cys Asp Leu Val His Thr Arg
165 170 175
Cys Val Ser Pro Thr Gly Thr His Thr Leu Leu Lys Lys Phe Pro Ala
180 185 190
Gln Lys Thr Asn Ser Ala Val Ser Leu Pro Phe Ser Val Val Cys Pro
195 200 205

Asp Ala Lys Thr Gln Cys Pro Asp Asp Ser Thr Cys Cys Glu Leu Pro
 210 215 220
 Thr Gly Lys Tyr Gly Cys Cys Pro Met Pro Asn Ala Ile Cys Cys Ser
 225 230 235 240
 Asp His Leu His Cys Cys Pro Gln Asp Thr Val Cys Asp Leu Ile Gln
 245 250 255
 Ser Lys Cys Leu Ser Lys Asn Tyr Thr Thr Asp Leu Leu Thr Lys Leu
 260 265 270
 Pro Gly Tyr Pro Val Lys Glu Val Lys Cys Asp Met Glu Val Ser Cys
 275 280 285
 Pro Glu Gly Tyr Thr Cys Cys Arg Leu Asn Thr Gly Ala Trp Gly Cys
 290 295 300
 Cys Pro Phe Ala Lys Ala Val Cys Cys Asp Asp His Ile His Cys Cys
 305 310 315 320
 Pro Ala Gly Phe Gln Cys His Thr Glu Lys Gly Thr Cys Glu Met Gly
 325 330 335
 Ile Leu Gln Val Gly Trp Met Lys Lys Val Ile Ala Pro Leu Arg Leu
 340 345 350
 Pro Asp Pro Gln Ile Leu Lys Ser Asp Thr Pro Cys Asp Asp Phe Thr
 355 360 365
 Arg Cys Pro Thr Asn Asn Thr Cys Cys Lys Leu Asn Ser Gly Asp Trp
 370 375 380
 Gly Cys Cys Pro Ile Pro Glu Ala Val Cys Cys Ser Asp Asn Gln His
 385 390 395 400
 Cys Cys Pro Gln Gly Phe Thr Cys Leu Ala Gln Gly Tyr Cys Gln Lys
 405 410 415
 Gly Asp Thr Met Val Ala Gly Leu Glu Lys Ile Pro Ala Arg Gln Thr
 420 425 430
 Thr Pro Leu Gln Ile Gly Asp Ile Gly Cys Asp Gln His Thr Ser Cys
 435 440 445
 Pro Val Gly Gln Thr Cys Cys Pro Ser Leu Lys Gly Ser Trp Ala Cys
 450 455 460
 Cys Gln Leu Pro His Ala Val Cys Cys Glu Asp Arg Gln His Cys Cys
 465 470 475 480
 Pro Ala Gly Tyr Thr Cys Asn Val Lys Ala Arg Thr Cys Glu Lys Asp
 485 490 495
 Val Asp Phe Ile Gln Pro Pro Val Leu Leu Thr Leu Gly Pro Lys Val
 500 505 510
 Gly Asn Val Glu Cys Gly Glu Gly His Phe Cys His Asp Asn Gln Thr
 515 520 525

Cys Cys Lys Asp Ser Ala Gly Val Trp Ala Cys Cys Pro Tyr Leu Lys
 530 535 540

Gly Val Cys Cys Arg Asp Gly Arg His Cys Cys Pro Gly Gly Phe His
 545 550 555 560

Cys Ser Ala Arg Gly Thr Lys Cys Leu Arg Lys Lys Ile Pro Arg Trp
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Asp Met Phe Leu Arg Asp Pro Val Pro Arg Pro Leu Leu
 580 585

<210> 3
 <211> 19
 <212> PRT
 <213> mouse granulin

<220>
 <221> PEPTIDE
 <222> (1)..(19)
 <223> Internal peptide of mouse GP88 used to raise the
 antisera against the GP88 used in the
 immunoaffinity step.

<400> 3
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 1 5 10 15

Ser Asp Thr

<210> 4
 <211> 12
 <212> PRT
 <213> mouse granulin

<220>
 <221> PEPTIDE
 <222> (1)..(12)
 <223> Internal peptide of mouse GP88 used to raise the
 antisera against the GP88 used in the
 immunoaffinity step.

<400> 4
 Pro Asp Ala Lys Thr Gln Cys Pro Asp Asp Ser Thr
 1 5 10

<210> 5
 <211> 14
 <212> PRT
 <213> mouse granulin

<220>
 <221> PEPTIDE
 <222> (1)..(14)
 <223> Internal peptide of mouse GP88 used to raise the
 antisera against the GP88 used in the
 immunoaffinity step.

<400> 5
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1 5 10

<210> 6
<211> 19
<212> PRT
<213> Human granulin

<220>
<221> PEPTIDE
<222> (1)..(19)
<223> Internal peptide of human GP88 used to develop
neutralizing anti-human GP88 monoclonal antibody.

<400> 6
Glu Lys Ala Pro Ala His Leu Ser Leu Pro Asp Pro Gln Ala Leu Lys
1 5 10 15
Arg Asp Val

A3
<210> 7
<211> 14
<212> PRT
<213> Human granulin

<220>
<221> PEPTIDE
<222> (1)..(14)
<223> Internal peptide of human GP88 used to develop
neutralizing anti-human GP88 monoclonal antibody.

<400> 7
Ala Arg Arg Gly Thr Lys Cys Leu Arg Arg Glu Ala Pro Arg
1 5 10

<210> 8
<211> 24
<212> DNA
<213> mammalian

<220>
<221> primer
<222> (1)..(24)
<223> Internal peptide of CMV promoter used as PCR
primer.

<400> 8
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24

<210> 9
<211> 27
<212> DNA
<213> mammalian

<220>
<221> primer
<222> (1)..(27)
<223> GP88 cDNA start codon used as oligonucleotide PCR
primer.

<400> 9
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27

<210> 10
<211> 27
<212> DNA
<213> mammalian

<220>
<221> primer
<222> (1)..(27)
<223> Antisense primer oligonucleotide primer

<400> 10
cgagaattca ggcagaccat gtgggtc

27

A3
<210> 11
<211> 23
<212> DNA
<213> mammalian

<220>
<221> primer
<222> (1)..(23)
<223> Antisense primer oligonucleotide primer

<400> 11
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23

<210> 12
<211> 25
<212> DNA
<213> mammalian

<220>
<221> primer
<222> (1)..(25)
<223> primer

<400> 12
ggatccacgg agttggttacc tgatc

25

<210> 13
<211> 25
<212> DNA
<213> mammalian

<220>
<221> primer
<222> (1)..(25)
<223> oligonucleotide PCR primer

<400> 13
gaattcgag gcagaccatg tggac

25

<210> 14
<211> 21
<212> DNA
<213> mammalian

<220>
<221> primer
<222> (1)..(21)
<223> Antisense oligonucleotide to human GP88

<400> 14
gggtccacat ggtctgcctg c

21

<210> 15
<211> 24
<212> DNA
<213> mammalian

A3
<220>
<221> primer
<222> (1)..(24)
<223> Antisense oligonucleotide to human GP88

<400> 15
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24

<210> 16
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<212> DNA
<213> Human GP88 cDNA

<220>
<221> CDS
<222> (13)..(1791)
<223> Nucleotide sequence of human granulin/epithelin
precursor (human GP88). Human Granulin Genbank
M75161.

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Leu Val Ala Gly Thr Arg Cys Pro Asp Gly Gln Phe Cys Pro Val Ala
15 20 25

tgc tgc ctg gac ccc gga gga gcc agc tac agc tgc tgc cgt ccc ctt 147
Cys Cys Leu Asp Pro Gly Gly Ala Ser Tyr Ser Cys Cys Arg Pro Leu
30 35 40 45

ctg gac aaa tgg ccc aca aca ctg agc agg cat ctg ggt ggc ccc tgc 195
Leu Asp Lys Trp Pro Thr Thr Leu Ser Arg His Leu Gly Gly Pro Cys
50 55 60

cag gtt gat gcc cac tgc tct gcc ggc cac tcc tgc atc ttt acc gtc 243
 Gln Val Asp Ala His Cys Ser Ala Gly His Ser Cys Ile Phe Thr Val
 65 70 75

tca ggg act tcc agt tgc tgc ccc ttc cca gag gcc gtg gca tgc ggg 291
 Ser Gly Thr Ser Ser Cys Cys Pro Phe Pro Glu Ala Val Ala Cys Gly
 80 85 90

gat ggc cat cac tgc tgc cca cgg ggc ttc cac tgc agt gca gac ggg 339
 Asp Gly His His Cys Cys Pro Arg Gly Phe His Cys Ser Ala Asp Gly
 95 100 105

cga tcc tgc ttc caa aga tca ggt aac aac tcc gtg ggt gcc atc cag 387
 Arg Ser Cys Phe Gln Arg Ser Gly Asn Asn Ser Val Gly Ala Ile Gln
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 Cys Pro Asp Ser Gln Phe Glu Cys Pro Asp Phe Ser Thr Cys Val
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 Cys Glu Asp Arg Val His Cys Cys Pro His Gly Ala Phe Cys Asp Leu
 160 165 170

gtt cac acc cgc tgc atc aca ccc acg ggc acc cac ccc ctg gca aag 579
 Val His Thr Arg Cys Ile Thr Pro Thr Gly Thr His Pro Leu Ala Lys
 175 180 185

aag ctc cct gcc cag agg act aac agg gca gtg gcc ttg tcc agc tcg 627
 Lys Leu Pro Ala Gln Arg Thr Asn Arg Ala Val Ala Leu Ser Ser Ser
 190 195 200 205

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 Val Met Cys Pro Asp Ala Arg Ser Arg Cys Pro Asp Gly Ser Thr Cys
 210 215 220

tgt gag ctg ccc agt ggg aag tat ggc tgc tgc cca atg ccc aac gcc 723
 Cys Glu Leu Pro Ser Gly Lys Tyr Gly Cys Cys Pro Met Pro Asn Ala
 225 230 235

acc tgc tgc tcc gat cac ctg cac tgc tgc ccc caa gac act gtg tgt 771
 Thr Cys Cys Ser Asp His Leu His Cys Cys Pro Gln Asp Thr Val Cys
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gac ctg atc cag agt aag tgc ctc tcc aag gag aac gct acc acg gac 819
 Asp Leu Ile Gln Ser Lys Cys Leu Ser Lys Glu Asn Ala Thr Thr Asp
 255 260 265

ctc ctc act aag ctg cct gcg cac aca gtg ggc gat gtg aaa tgt gac 867
 Leu Leu Thr Lys Leu Pro Ala His Thr Val Gly Asp Val Lys Cys Asp
 270 275 280 285

atg gag gtg agc tgc cca gat ggc tat acc tgc tgc cgt cta cag tcg 915
 Met Glu Val Ser Cys Pro Asp Gly Tyr Thr Cys Cys Arg Leu Gln Ser
 290 295 300

ggg gcc tgg ggc tgc tgc cct ttt acc cag gct gtg tgc tgt gag gac 963
 Gly Ala Trp Gly Cys Cys Pro Phe Thr Gln Ala Val Cys Cys Glu Asp
 305 310 315

cac ata cac tgc tgt ccc gcg ggg ttt acg tgt gac acg cag aag ggt 1011
 His Ile His Cys Cys Pro Ala Gly Phe Thr Cys Asp Thr Gln Lys Gly
 320 325 330

acc tgt gaa cag ggg ccc cac cag gtg ccc tgg atg gag aag gcc cca 1059
 Thr Cys Glu Gln Gly Pro His Gln Val Pro Trp Met Glu Lys Ala Pro
 335 340 345

gct cac ctc agc ctg cca gac cca caa gcc ttg aag aga gat gtc ccc 1107
 Ala His Leu Ser Leu Pro Asp Pro Gln Ala Leu Lys Arg Asp Val Pro
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tgt gat aat gtc agc agc tgt ccc tcc tcc gat acc tgc tgc caa ctc 1155
 Cys Asp Asn Val Ser Ser Cys Pro Ser Ser Asp Thr Cys Cys Gln Leu
 370 375 380

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 Thr Ser Gly Glu Trp Gly Cys Cys Pro Ile Pro Glu Ala Val Cys Cys
 385 390 395

A3 tgc gac cac cag cac tgc tgc ccc cag cga tac acg tgt gta gct gag 1251
 Ser Asp His Gln His Cys Cys Pro Gln Arg Tyr Thr Cys Val Ala Glu
 400 405 410

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 Pro Ala Arg Arg Gly Ser Leu Ser His Pro Arg Asp Ile Gly Cys Asp
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 Gln His Thr Ser Cys Pro Val Gly Gly Thr Cys Cys Pro Ser Gln Gly
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 Gly Ser Trp Ala Cys Cys Gln Leu Pro His Ala Val Cys Cys Glu Asp
 465 470 475

cgc cag cac tgc tgc ccg gct ggc tac acc tgc aac gtg aag gct cga 1491
 Arg Gln His Cys Cys Pro Ala Gly Tyr Thr Cys Asn Val Lys Ala Arg
 480 485 490

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 Ser Cys Glu Lys Glu Val Val Ser Ala Gln Pro Ala Thr Phe Leu Ala
 495 500 505

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 Arg Ser Pro His Val Gly Val Lys Asp Val Glu Cys Gly Glu Gly His
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Ala Cys Cys Pro Tyr Ala Gln Gly Val Cys Cys Ala Asp Arg Arg His
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Cys Cys Pro Ala Gly Phe Arg Cys Ala Arg Arg Gly Thr Lys Cys Leu
560 565 570

cgc agg gag gcc ccg cgc tgg gac gcc cct ttg agg gac cca gcc ttg 1779
Arg Arg Glu Ala Pro Arg Trp Asp Ala Pro Leu Arg Asp Pro Ala Leu
575 580 585

aga cag ctg ctg tgaggacag tactgaagac tctgcagccc tcgggacccc 1831
Arg Gln Leu Leu
590

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<211> 593
<212> PRT
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Asp Pro Gly Gly Ala Ser Tyr Ser Cys Cys Arg Pro Leu Leu Asp Lys
35 40 45

Trp Pro Thr Thr Leu Ser Arg His Leu Gly Gly Pro Cys Gln Val Asp
50 55 60

Ala His Cys Ser Ala Gly His Ser Cys Ile Phe Thr Val Ser Gly Thr
65 70 75 80

Ser Ser Cys Cys Pro Phe Pro Glu Ala Val Ala Cys Gly Asp Gly His
85 90 95

His Cys Cys Pro Arg Gly Phe His Cys Ser Ala Asp Gly Arg Ser Cys
100 105 110

Phe Gln Arg Ser Gly Asn Asn Ser Val Gly Ala Ile Gln Cys Pro Asp
115 120 125

Ser Gln Phe Glu Cys Pro Asp Phe Ser Thr Cys Cys Val Met Val Asp
130 135 140

Gly Ser Trp Gly Cys Cys Pro Met Pro Gln Ala Ser Cys Cys Glu Asp
 145 150 155 160
 Arg Val His Cys Cys Pro His Gly Ala Phe Cys Asp Leu Val His Thr
 165 170 175
 Arg Cys Ile Thr Pro Thr Gly Thr His Pro Leu Ala Lys Lys Leu Pro
 180 185 190
 Ala Gln Arg Thr Asn Arg Ala Val Ala Leu Ser Ser Ser Val Met Cys
 195 200 205
 Pro Asp Ala Arg Ser Arg Cys Pro Asp Gly Ser Thr Cys Cys Glu Leu
 210 215 220
 Pro Ser Gly Lys Tyr Gly Cys Cys Pro Met Pro Asn Ala Thr Cys Cys
 225 230 235 240
 Ser Asp His Leu His Cys Cys Pro Gln Asp Thr Val Cys Asp Leu Ile
 245 250 255
 Gln Ser Lys Cys Leu Ser Lys Glu Asn Ala Thr Thr Asp Leu Leu Thr
 260 265 270
 Lys Leu Pro Ala His Thr Val Gly Asp Val Lys Cys Asp Met Glu Val
 275 280 285
 Ser Cys Pro Asp Gly Tyr Thr Cys Cys Arg Leu Gln Ser Gly Ala Trp
 290 295 300
 Gly Cys Cys Pro Phe Thr Gln Ala Val Cys Cys Glu Asp His Ile His
 305 310 315 320
 Cys Cys Pro Ala Gly Phe Thr Cys Asp Thr Gln Lys Gly Thr Cys Glu
 325 330 335
 Gln Gly Pro His Gln Val Pro Trp Met Glu Lys Ala Pro Ala His Leu
 340 345 350
 Ser Leu Pro Asp Pro Gln Ala Leu Lys Arg Asp Val Pro Cys Asp Asn
 355 360 365
 Val Ser Ser Cys Pro Ser Ser Asp Thr Cys Cys Gln Leu Thr Ser Gly
 370 375 380
 Glu Trp Gly Cys Cys Pro Ile Pro Glu Ala Val Cys Cys Ser Asp His
 385 390 395 400
 Gln His Cys Cys Pro Gln Arg Tyr Thr Cys Val Ala Glu Gly Gln Cys
 405 410 415
 Gln Arg Gly Ser Glu Ile Val Ala Gly Leu Glu Lys Met Pro Ala Arg
 420 425 430
 Arg Gly Ser Leu Ser His Pro Arg Asp Ile Gly Cys Asp Gln His Thr
 435 440 445
 Ser Cys Pro Val Gly Gly Thr Cys Cys Pro Ser Gln Gly Gly Ser Trp
 450 455 460

Ala Cys Cys Gln Leu Pro His Ala Val Cys Cys Glu Asp Arg Gln His
465 470 475 480

Cys Cys Pro Ala Gly Tyr Thr Cys Asn Val Lys Ala Arg Ser Cys Glu
485 490 495

Lys Glu Val Val Ser Ala Gln Pro Ala Thr Phe Leu Ala Arg Ser Pro
500 505 510

His Val Gly Val Lys Asp Val Glu Cys Gly Glu Gly His Phe Cys His
515 520 525

Asp Asn Gln Thr Cys Cys Arg Asp Asn Arg Gln Gly Trp Ala Cys Cys
530 535 540

Pro Tyr Ala Gln Gly Val Cys Cys Ala Asp Arg Arg His Cys Cys Pro
545 550 555 560

Ala Gly Phe Arg Cys Ala Arg Arg Gly Thr Lys Cys Leu Arg Arg Glu
565 570 575

Ala Pro Arg Trp Asp Ala Pro Leu Arg Asp Pro Ala Leu Arg Gln Leu
580 585 590

Leu